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Clinical Trial Summary

Phase I/II Trial of S64315 Plus Azacitidine in Acute Myeloid Leukaemia

Full scientific title: Phase I/II, international, multicentre, open-label, non-randomised, non-comparative study evaluating the safety, tolerability and clinical activity of intravenously administered S64315, a selective Mcl-1 inhibitor, in combination with azacitidine in patients with acute myeloid leukaemia (AML)

We thank all the participants who took part in the study. Clinical study participants are very important for making progress in science, for the benefit of patients.
This document is a summary of the study. It is written for a general audience.

Researchers need many studies to decide which medicines work the best and are the safest for patients. For medical science to progress, many studies involving patients are running all around the world. This summary only shows the results from this one study. Other studies, evaluating the same drug, may find different results. You should not change your current treatment based on the results of this single study. If you have any questions about this study, please talk to your doctor.

Therapeutic area:
Oncology

Disease:
Acute Myeloid Leukaemia (AML)

Study phase:
Phase I/II

Final version 2
21/02/2024

In this summary:

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1 Why was this study done?

This study was done to test a new anticancer drug, S64315, combined with another anticancer drug, azacitidine, in participants with acute myeloid leukaemia (AML).

AML is a rapidly progressing cancer of the blood and bone marrow. In AML, the cancer cells have higher amounts of certain proteins such as Mcl-1 (myeloid cell leukaemia 1). These Mcl-1 proteins promote the survival of cancer cells.

S64315 is a drug that blocks Mcl-1 proteins. This blocking leads to the death of the cancer cells.

In this study, S64315 was combined with another drug called azacitidine. S64315 and azacitidine are referred to here as 'study drugs'. Azacitidine is already approved for the treatment of AML. Azacitidine works by interacting with the DNA (genetic material), helping the destruction of cancer cells. It was hoped that by combining S64315 and azacitidine, their actions on the cancer cells might be more effective.

Two parts were planned in this study. The main objective of the first part was to look at the safety of S64315 when given in combination with azacitidine. The main objective of the second part was to assess how many patients showed no signs of AML after treatment with S64315 in combination with azacitidine.

2 When and where did this study take place?

When did the study take place?

- This study started in February 2021.
- It ended in August 2023.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Spain	10
France	3
Australia	2
United States of America	2

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to:

- Be at least 18 years old.
- Have AML
  - that returned after improvement (relapsed) or did not respond to any treatment (refractory) and for which there was no other approved therapy that could be prescribed, or
  - secondary to a condition called myelodysplastic syndrome, in which the bone marrow does not make enough healthy blood cells.

How many participants took part in the study?

A total of 17 participants took part in the study (first part only): 7 women and 10 men. The second part of the study was not started due to the stop of the study during the part one (see explanations in section 7 of this summary).

How old were the participants?

The average age of the participants was 65 years. The youngest participant was 42 years old and the oldest was 80 years old.

4 Which treatments did the participants receive?

All participants received a combination of S64315 and azacitidine.

- S64315 was given through infusion (injection given slowly) into a vein at doses ranging from 25 milligrams (mg) to 190 mg. Infusion time was at least 2 hours.
- Azacitidine was given as an injection under the skin at a fixed dose of 75 mg/m².

The participants took S64315 alone once a week for 2 weeks. Then, they took a combination of S64315 once a week and azacitidine once a day from Day 1 to Day 7 over periods of treatment called 'cycles'. One cycle lasted 28 days.

These 28-day cycles were repeated for as long as:

- the cancer did not progress,
- the treatment was working for the participant,
- the participant did not have too severe side effects.

The participant could also decide to stop the treatment at any time.

5 How was the study carried out?

The study is called an "open-label" study. This means that both the participants and the research doctors knew which treatment was taken.

The participants started with a first period called an inclusion period that lasted up to 15 days. This period allowed doctors to check if the participant fulfilled the criteria (see section 3) to take part in the study and could receive the study treatment.

Then, the participants were included in the study and started treatment.

To find the highest tolerated dose of the combination, the doctors tested different doses of S64315 (with the fixed dose of azacitidine) in small groups of participants. The first group received the lowest dose, and then each new group received a higher dose. For each dose, the doctors checked the safety of the study drugs. Then, the researchers decided whether to increase the dose of S64315 in the next group of participants.

It was planned that once the highest tolerated dose was found, the researchers defined the recommended dose for study part II (dose that is both safe and effective for participants).

The participants visited the doctors regularly. During the visits, the doctors collected information about the participants' health.

6 What were the side effects?

Side effects are unwanted medical events that the doctors think may be caused by the treatments in the study.

In this summary, we describe unwanted medical events thought to be caused by S64315 or azacitidine.

The results may be presented differently in other documents related to the study.

The table below shows the number of participants who had side effects.

	Out of 17 participants
Participants who had side effect(s)	14 (82%)
Participants who had serious* side effect(s)	3 (18%)
Participants who stopped the treatment because of side effect(s)	1 (6%)

**See definition of serious side effects below*

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What were the types of side effects?

The table below shows the most common side effects reported in the study (reported by at least 10% of participants).

	Out of 17 participants
Increase in liver enzyme called ALT	6 (35%)
Increase in liver enzyme called AST	5 (29%)
Constipation	4 (24%)
Increase in blood levels of bilirubin, indicating liver problems	2 (12%)
Increase in troponin "T" possibly indicating a heart injury	2 (12%)
Diarrhoea	2 (12%)
Feeling sick	2 (12%)

= *participants*

What were the serious side effects?

A side effect is considered serious when:

- the participant needs to be hospitalised,
- it causes lasting damage or death,
- the participant's life is in danger or,
- it is medically important in the doctor's opinion.

The table below shows the serious side effects reported in this study.

	Out of 17 participants
Increase in liver enzyme called ALT	1 (6%)
Increase in liver enzyme called AST	1 (6%)
Increase in blood levels of bilirubin, indicating liver problems	1 (6%)
Increase in troponin "I" possibly indicating a heart injury	1 (6%)
Low level of neutrophils, a type of white blood cells	1 (6%)

= *participants*

In the study, no participants died because of an unwanted event thought to be caused by S64315 or azacitidine.

7 What were the study results?

During the first part of the study, the sponsor (the company that organised and funded the research) decided to stop the study. This decision was based on limited positive effects of the study drugs observed in most participants of the first part. Therefore, the second part of the study was not started. This decision was not due to safety problems with the study drugs.

This document presents only the results for the main objective of the first part of this study. Other results are available in other documents listed in section 10.

The safety results of the study drugs are described in section 6 of this summary.

Due to the stop of the study, the highest tolerated dose of S64315 in combination with azacitidine was not reached, and the recommended dose could not be determined.

8 How has this study helped research?

The study helped researchers to gather more information on the safety of the S64315 combined with azacitidine. This study also helped researchers in their understanding of the effects of S64315 in combination with azacitidine in AML treatment.

This summary shows only the main results from this one study. Other studies, evaluating the same drug, may find different results.

9 Are there plans for further studies?

No other studies with S64315 are planned so far.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL1-64315-004
- EudraCT number: 2019-004896-38
- NCT number: NCT04629443

Who did the study?

The company that organised and funded the research, called the "sponsor", is the Institut de Recherches Internationales Servier based in Suresnes Cedex, France.

How can you contact the sponsor?

Contact us on Servier website
https://servier.com/en/

Where can you learn more about this study?

You can find more information about this study on these websites:

- https://clinicaltrials.servier.com/find-clinical-trials
- http://www.clinicaltrialsregister.eu/ctr-search
- www.clinicaltrials.gov

In this document we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary at
https://clinicaltrials.servier.com/glossary/

You can find general information about clinical trials on https://clinicaltrials.servier.com/